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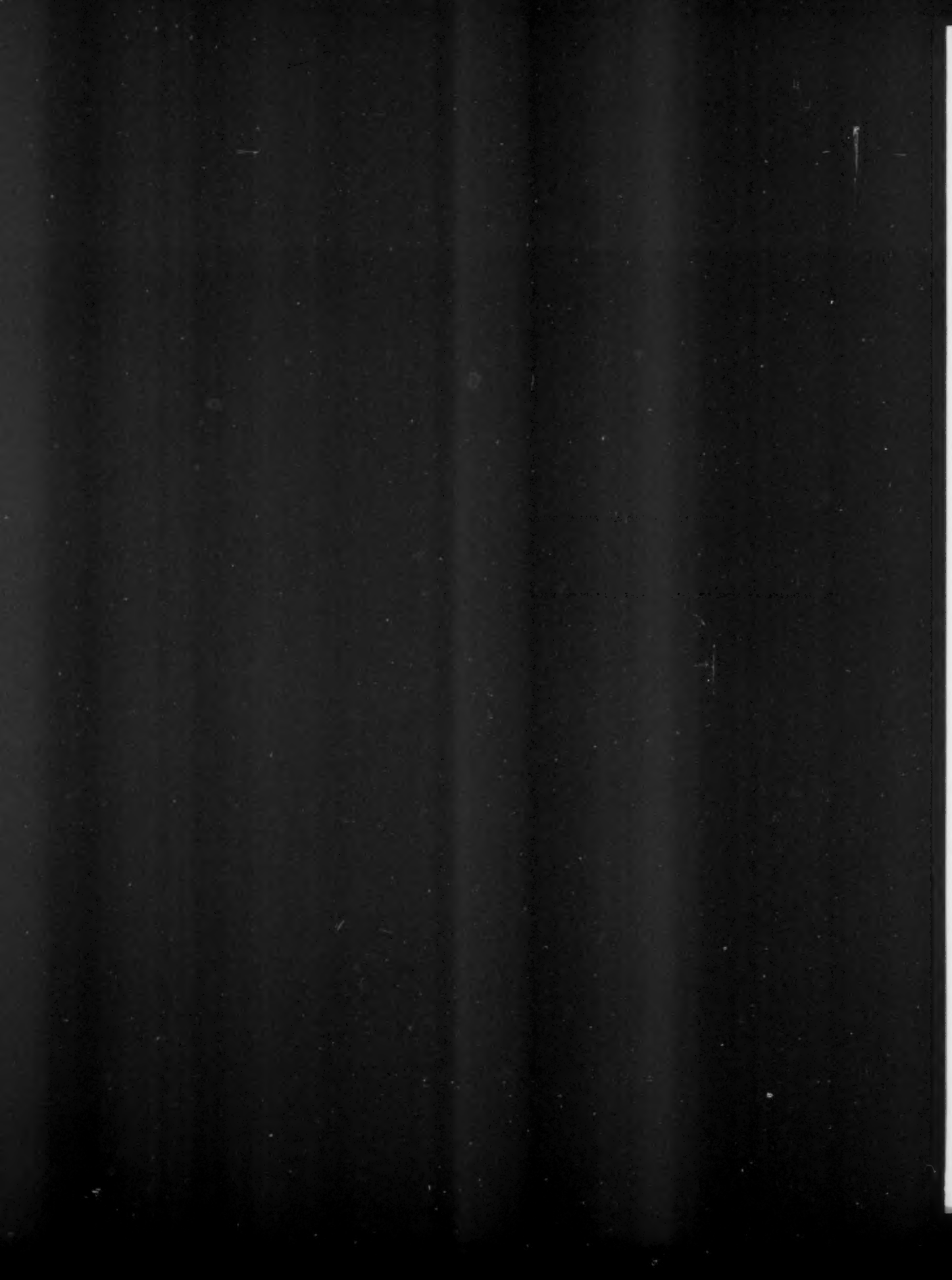
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Special Issue on Bone Fluid Flow: Organ to Cell, Lab Bench to Bedside, On Earth and In Space

Guest Editor: Melissa L. Knothe Tate

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**Cover:** This special issue of the *Annals of Biomedical Engineering* addresses bone fluid flow at multiple length scales. Bone tissue and cells are uniquely challenging to study due to the nature of the mineralized matrix and cells therein. Adopting one of nature's most challenging tissues as a model provides a "robust testbed" for future application to non-skeletal tissues as well. Osteocytes are entombed in the bone matrix within lacunae that are lined with collagen (vertical fibrils observed in left half of 10  $\mu\text{m}$  image). The osteocyte body and its multiple dendritic processes are surrounded by a pericellular network contained within the lacunar and canalicular spaces of the mineralized extracellular matrix that defines the boundary conditions for flow in the periosteocytic space. The boundary of the periosteocytic flow volume is leaky, tortuous, branches into finer conduits, and has a matrix wall roughness up to half the average diameter of the annulus (observed in the 1  $\mu\text{m}$  image of a cell process in the plane and one orthogonal to the plane of the page). Computational fluid dynamics models of periosteocytic flow show different flow regimes in the vicinity of the cell body, where the organelles are housed, compared to those along the cell processes that are joined by gap junctions. (See Article by Anderson et al., p. 52).

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**Cover:** Gene therapy designed to limit intimal hyperplasia is a promising method for improving the long-term patency of saphenous veins used as coronary artery bypass grafts. The pressure-induced transport of adenovirus-sized particles was studied by quantifying the presence of fluorescent nanospheres in the intimal and medial layers of isolated human saphenous vein segments perfused ex vivo. Cover image illustrates 100 nm diameter nanospheres (red) lining the intima after one hour of pressurization at 400 mmHg. Few nanospheres are seen in the media where smooth muscle cells are abundant (nuclei stained green). The ex vivo perfusion experiment is an ideal way to quantify vein permeability and optimize gene therapy delivery protocols in human tissue. (See Ander et al., p. 202).

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Cover: Adipocyte specific staining was performed on human bone marrow stromal cells after adipogenic differentiation. Positive reaction expressed by red staining indicates intracellular lipid storage, a specific morphological characteristic of adipogenesis.

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*Cover:* The three-dimensional arrangements of muscle fibers are shown here for the gluteus maximus, a hip extensor muscle. This muscle wraps around underlying structures and has broad attachments. By combining this description of fiber arrangements with a finite-element mesh of this muscle and a nonlinear transversely-isotropic constitutive model for muscle, we simulated the behavior of the muscle through a range of hip motion. This revealed that fibers within the muscle had a broad range of behaviors.

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**Cover:** A three-dimensional computer graphics based model of the upper limb. The model includes 50 muscles and 15 degrees of freedom representing the joints from the shoulder to fingertip. The best available data representing the joint kinematics, muscle moment arms, and muscle force-generating characteristics were integrated into this biocomputational model to capture the essential features of upper limb mechanics. The model facilitates the study of neuromuscular control and analysis of surgical procedures of the upper limb.

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Cover: Typical bone cell adhered to fibronectin or glass imaged using an atomic force microscope (left, image width = 100 $\mu$ m). Filamentous actin (center, green) and microtubule (right, red) cytoskeleton staining of bone cells adhered to fibronectin or glass (bar = 20 $\mu$ m).

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Cover: Spatially aligned macroscopic tissue (left) and Masson trichrome stained histology (right) images of rabbit thigh muscle following radio-frequency thermal ablation. the thermal lesion is the elliptical region that has a dark brown rim in tissue and a purple stained region of necrosis in histology. The boundary of cell death (yellow) was marked in the histology and copied to microscopic tissue image. Needle tracks (arrows) used for image registration (circles) and validation (squares) were copied to both images Excellent registration accuracy of tissue and histology images is clearly evident with good correspondence of needle tracks. (See article by Breen et al.).

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**Cover:** The hemodynamics in the arterial anastomosis of a loop polytetrafluorethylene graft used as vascular access for hemodialysis. The path lines colored by velocity in the arterial anastomosis of a 6 mm graft (left top panel) and in the arterial anastomosis of a 4–7 mm graft (right top panel). The wall shear stress (WSS) at the arterial anastomosis of the 6 mm graft (left bottom panel) and at the arterial anastomosis of the 4–7 mm graft (right bottom panel).

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Cover: Top row: Proton density, T2 weighted and fluid attenuation inversion recovery sequence Magnetic Resonance images corresponding to brain cross-section of a multiple sclerosis subject. Bottom row: First three images are preprocessed and extrameningeal tissue removed images of top row. The last image is the segmented image obtained by three dimensional KNN algorithm. Different segmented tissues shown are Blue: Cerebrospinal Fluid, Pink: White Matter, Gray: Gray Matter, Yellow: Multiple Sclerosis Lesions. (See article by Renjie He et al. on page 1439)

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Cover: Migration of cultured aortic Vascular Smooth Muscle Cells (VSMC) from transgenic mice (Tgp22<sup>phox</sup>), in which p22<sup>phox</sup> is overexpressed, was visualized focusing on wound edge (white dashed line) area. Cells were stained by Myosin Heavy Chain embryonic (SMemb) immunocytochemistry (red colored, left figure). The white arrow indicates migration direction toward the wound-scratched area. The image was converted from plain (left figure) to range scaled plate (right figure) to indicate the level of fluorescence intensity representing SMemb expression in each single cell. The continuous color change from blue to red represents expression of SMemb from low to high levels. Mostly, VSMC at the wound area showed higher SMemb expression than non-migration area.

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Special Issue: International Biofluid Mechanics Symposium

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